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A Measles Epidemic in an Alaskan Boarding School

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A measles epidemic occurred among Aleut, Eskimo and Indian students at the Mt. Edgecumbe School,, Sitka, Alaska, in 1962. Confirmed cases were virtually confined to students from several isolated communities where measles had not occurred for many years. All serologically susceptible individuals showed some evidence of measles infection. In a small group, superinfection with measles virus was observed among serologically immune students who did not develop clinical measles.

Gamma globulin modified the severity of measles to some degree. Antibody levels were significantly lower in the group that received gamma globulin in the period from three days before to two days after the appearance of rash, suggsting a possible interference with normal antibody development.

An epidemic of measles occurred at the Mt. Edgecumbe School, Sitka, Alaska, in September, 1962, involving 10 per cent of the school's 669 students. Blood specimens were collected from most of the students two weeks prior to the epidemic and, during the latter days of the epidemic, all students were tuberculin tested. Gamma globulin was given prophylactically to most students early in the epidemic. This unique combination of events provided an opportunity to study measles in a high school population, in terms of infectiousness of the virus and the effects of gamma globulin prophylaxis. An analysis of data concerning tuberculin responses will be presented separately.[1]

background

The Mt. Edgecumbe School, administered by the Bureau of Indian Affairs, draws its student body from the Aleut, Eskimo and Indian populations throughout Alaska. The school offers a four-year high school program. Students reside in dormitories during the school term and customarily return to their native villages in the summer.

The institution is located on Japonski Island, in Sitka Sound, several hundred feet from the coastal community of Sitka. Also located on this Island is the Mt. Edgecumbe Hospital, a large Public Health Service facility, with 250 beds and a permanent staff of nine physicians, one of whom is assigned to the school clinic. Students, when ill, report to the clinic or are directed to report to the physician by dormitory supervisors.

Early in August, 1962, measles appeared in the community of Sitka. On September 7, the first case was noted in a student at the Mt. Edgecumbe School. Within seven days, four more cases occurred and then the illness disseminated rapidly through the school. The last measles case was reported on October 5.

materials and methods

Clinical cases of measles were diagnosed by a physician. In many instances the children were hospitalized, although shortage of hospital beds made it necessary for some of the ill students to remain in their dormitories.

Gamma globulin was administered prophylactically (and in some instances, after actual onset of symptoms), 0.02 ml per lb (0.044 ml per kg), to 642 of the 669 students. Most of the gamma globulin was dispensed between September 16-23.

An attempt was made to review the clinical records six months after the outbreak in order to establish the diagnosis and to classify cases in terms of severity of symptoms. Because of the fact that daily temperatures were not available from patients who were not hospitalized, this breakdown was not satisfactory. The term *severe measles* in the text refers to cases in individuals

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who were hospitalized and assigned this designation retrospectively by the admitting physician. Final diagnosis of measles was difficult to assess since, toward the end of the epidemic, after gamma globulin was administered, minimal and questionable symptoms appeared in many students. To resolve the problem of diagnosis we relied primmarily on serologic studies. The term *confirmed measles* in the text refers to those with clinical and serologic evidence of disease.

Blood specimens were collected during the last week in August, 1962, and again during the first week of April, 1963, from 588 of the 669 students. Subsequent analysis is based on this group. All specimens were tested for hemagglutination inhibition (HI) antibody at the Arctic Health Research Center, PHS, Anchorage. Tests were performed by the method of Rosen with the following modifications.[2] A 1:5 dilution of serum was prepared and extracted by adding 0.2 ml of serum to 0.8 ml of a 25 per cent kaolin slurry in saline. Material remained at room temperature with occasional shaking for 20 minutes at which time the tubes were centrifuged for five minutes at 2000 RPM to separate the kaolin. Instead of transferring the supernate to another test tube, rhesus monkey erythrocytes (0.1 ml of a 50 per cent suspension in saline) were added directly to the serum and kaolin. The tubes were agitated gently and placed at 4 C for one hour and then centrifuged for 10 minutes at 2000 RPM. Erythrocytes and kaolin formed a tight precipitate with minimal hemolysis leaving an almost straw-colored supernate that was poured off. All sera were tested in one continuous run using hemagglutinating antigen purchased from a commercial source.*

Selected sera were re-extracted and tested a second time to explore unusual serologic reactions. For these tests, sensitivity of the HI system was increased by using an aliquot of a 1:5 serum dilution and titering it in the presence of 1, 2, and the usual 4 units of hemagglutinin. To demonstrate the specificity of measles antibody when challenged with less than 4 units of hemagglutinin, we tested 10 pre-epidemic sera from confirmed measles cases and, in addition, 20 sera collected during another study[3] among measles susceptible individuals residing in an area where canine distemper was endemic.[4] In no instance did we observe antibody in these sera when tested with 1 or 2 units of hemagglutinin. Among individuals with measles antibody, our findings were generally similar to those reported by Togo who showed a fourfold rise of measles HI titer with every twofold decrease in units of antigens.[5]

*Microbiological Associates, Bethesda, Maryland.

results

Confirmed measles occurred in 58 of 588 students from whom paired blood specimens were available. Severe measles was observed in 22 students while the remainder of the cases varied in severity from moderately severe disease to very mild illness in which only a fleeting rash was noted. Severe cases tended to occur earlier in the epidemic, (Figure 1). First cases were among males and the peak among males came somewhat earlier than that among females.

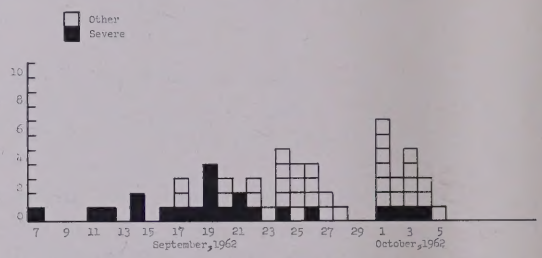

Fig. 1. Measles cases, Mt. Edgecumbe—Epidemic curve—58 confirmed cases.

Confirmed measles cases occurred in clusters among students from several relatively isolated Alaskan communities where measles had been absent for many years. In 20 instances the diagnosis of measles was made in individuals who did not reside in villages in which other cases were reported. The symptoms in these cases were mild and in each instance significant antibody was present in the pre-epidemic serum and serologic rise did not occur. These 20 indivduals are not included on the graph in Figure 1.

No demonstrable antibody to measles was found in 63 students prior to the epidemic, even when tested against 1 unit of hemagglutinin. All had titer in the post epidemic bleeding. Clinical measles was diagnosed in 58 of the 63. Final titer and severity of illness are shown on Table 1. Clinical measles was not diagnosed in five of the 63 students. Their final titers were very low; three of the five having antibody that was detected only by using 1 or 2 units of hemagglutinin. All five were from villages in which other measles cases did not occur, and three were from the same village.

Of the 525 students in whom antibody to measles was present prior to the epidemic (Table

TABLE 1. Clinical and serologic findings among students with no measles antibody before the epidemic.

Final titer	No measles	Measles Severe	Measles Other	Total
Detectable only vs. less than 4 units	3			3
5	1	1	3	5
10	1	4	5	10
20		8	15	23
40		6	8	14
80		3	4	7
160			1	1
Totals	5	22	36	63

TABLE 2. Clinical and serologic findings among students with measles antibody before the epidemic.

Pre-epidemic titer	Fourfold or greater serologic rise	No fourfold serologic rise	Total
Detectable only vs. less than 4 units	12	15	27
5	2	90	92
10		135	135
20		123	123
40		96	96
80		43	43
160		9	9
Totals	14	511	525

2,) a fourfold rise in titer was demonstrated in 14. Symptoms were not encountered in this group. The initial titers in these 14 individuals were consistently low, with 12 having antibody detectable only by using 1 or 2 units of hemagglutinin.

Gamma globulin appeared to modify the severity of symptoms when given early in the incubation period, (Figure 2). Of 58 confirmed

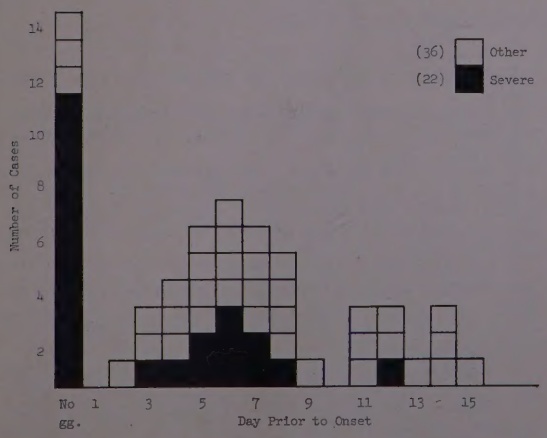

Fig. 2. Timing of receipt of gamma globulin and severity of illness.

cases 22 were severe. Eleven of these did not receive gamma globulin prior to onset of symptoms, while in nine instances symptoms developed within seven days of inoculation. Among 36 confirmed measles cases which were not severe, 15 received gamma globulin at least eight days prior to onset of rash.

The final titers of those who received gamma globulin before onset of symptoms were slightly higher than among those who did not receive gamma globulin or received gamma globulin after onset of symptoms (Table 3), but the difference was not significant ($P > .10$) when analyzed by the X^2 test. A significant difference was encountered, however, among those who received gamma globulin from three days before onset of rash to two days after onset of rash ($P > .01$).

discussion

The epidemic of measles in an Alaskan boarding school provided an opportunity to investigate serologic patterns in an unusual population which was somewhat older than most groups similarly studied. We were limited in our clinical evaluation since data were secured from hospital records six months after the outbreak and information on patients who were not hospitalized was incomplete. Widespread use of gamma globulin further complicated diagnosis.

Our data emphasize the great infectiousness of measles virus. All seronegative individuals developed antibody during the course of the outbreak. In five instances clinical symptoms did not appear among students without demonstrable antibody prior to the epimedic. These students all had received gamma globulin. Inapparent measles after modifying dose of gamma globulin has been reported by Black and Yannet.[6] While this may be the explanation for the failure of symptoms to develop in these five students, we were more impressed by the fact that only five students of the 63 serologic susceptibles were from villages in which other clinical cases did not occur and all showed minimal antibody responses. It is likely that these students had partial immunity which could not be detected by our serologic tests and upon re-exposure to measles had a booster phenomenon with subclinical infection which has been reported by Stokes *et al.*[7] and Krugman *et al.*[8] If we accept this explanation for the patterns in these five students, we can conclude that all truly susceptible students developed clinically apparent measles.

A fourfold or greater rise in antibody level occurred among 14 students in whom antibody was detected in the pre-epidemic bleeding. These

TABLE 3. Measles cases in terms of titer, onset of symptoms and timing of gamma globulin administration.

HI TITER	Onset of Symptoms								
160						1			
80						3	2	1	1
40	2	1				2	4	2	2
20	1		1	6	1	8	3	3	
10				2	2	3	1		1
5				1	1		2		1
	No gg.	9-6	5-3	2-0	1-3	4-6	7-9	10-12	13-15
	Days before receiving gg.					Days after receiving gg.			

children were asymptomatic and were from villages in which other students did not develop clinical symptoms. The rise in antibody in this group is another indication of subclinical, superinfection. Stokes *et al.*[7], using complement fixation and neutralizing antibody, and Krugman *et al.*[8], using HI antibody, noted that subclinical superinfection is dependent upon initial titer. This was strikingly the case in the present series since booster effects occurred only among those with very low antibody levels. Krugman *et al.*[8], have shown that HI antibody response to this booster is maximal after 12 days and then gradually declines. Since the second blood specimen was not collected for six months, it is possible that others with serologic rises were missed. Our findings support the thesis that in a small number of individuals subclinical, superinfections with measles virus occur.

Gamma globulin appeared to modify clinical severity of measles. Most of the severe cases had not received gamma globulin or received it late during the incubation period.

Those who received gamma globulin before onset of rash had slightly higher titers than those who did not receive gamma globulin at all, or those who received it after onset of symptoms. This difference was not statistically significant. Significantly lower titers appeared, however, among those who received gamma globulin during the period from three days before to two days after onset of rash. Since antibody to measles appears within a day or two after onset of symptoms, it may be that gamma globulin, when present in high concentration during this period, is capable of suppressing part of the normal antibody formation. It has been shown that large doses of passively administered 7S antibody (the active component in gamma globulin) inhibits antibody formation in laboratory animals.[9] ■

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abstracto

Una epidemia de sarampión ocurrió entre estudiantes, Aleutianos, Esquimales e Indios en Mt. Edgecumbe School, Sitka, Alaska, en 1962. Casos confirmados fueron virtualmente confinados a estudiantes de varias comunidades aisladas donde el sarampión no ha ocurrido por muchos años. Todos los individuos susceptibles serologicamente mostraron alguna evidencia de infeción sarampionosa. En un pequeño grupo, superinfecciónе con virus del sarampión fue observado entre estudiantes inmunes serologicamente, quienes no desarrollaron sintomatolgía sarampionosa.

Gamma globulina modificó la severidad del sarampión en elgun grado. Niveles de anticuerpos fueron significamente más bajos en el groupo que recibió gamma globulina en el periodo desde tres dias antes a dos dias despues de la aparición del rash, sugiriendo una posible inferencia con el normal desarollo de anticuerpos.

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